ANTIARRHYTHMIC DRUGS

A. Actuality. Cardiac arrhythmias are some of the most common symptoms of cardiovascular diseases, acute intoxications, etc., which in turn can cause severe cardiodynamic and systemic hemodynamic disturbances, often being a major factor in lethality. The treatment of cardiac arrhythmias is a problem of major importance for medical practice and requires knowledge of the pharmacokinetic and pharmacodynamic aspects of antiarrhythmic drugs.

B. The purpose of the training is: familiarization of the student with the pharmacological properties of antiarrhythmic drugs.

C. Learning objectives:

1) The student **must know:** the name of the main antiarrhythmic drugs, the principles of classification, pharmacokinetic aspects, the mechanism of action and pharmacological effects, indications and contraindications, adverse reactions, optimal routes of administration depending on the situation.

2) The student **must be able to:** prescribe antiarrhythmic drugs in all forms of delivery, indicate drugs in various heart rhythm disorders, apply the acquired knowledge to solving situational problems.

D. Knowledge from previous and tangential disciplines necessary for interdisciplinary integration.

Human anatomy. Heart – functional anatomy, abnormalities.

Histology and embryology. Heart. Development, structure, histophysiology. Age-related changes in the heart.

Biophysics. Bioelectric phenomena. Membrane potential.

Biochemistry. Structural organization of biological membranes.

Physiology. Rhythmic excitement of the heart. Normal electrocardiogram. The principles of vector analysis of the electrocardiogram. Electrocardiographic interpretation of cardiac conditions.

Toxicology. Toxins and drugs that cause cardiac arrhythmias.

The pathophysiology. Pathogenic chain of compensatory reactions and blood circulation disturbances in heart rhythm disorders.

Semiology - internal medicine. Tachycardia, bradycardia, sinus arrhythmia, extrasystole, atrial and ventricular flutter, atrial and ventricular fibrillation, atrioventricular block.

E. Self-training questions:

1. Definition and classification of antiarrhythmic drugs.
2. Drugs used in tachyarrhythmias and extrasystoles: classification.
3. Drugs that block ion channels of cardiomyocytes, classification.
4. Sodium channel blockers (membrane stabilizers): mechanism of action.

a. Subclass IA (quinidine group): antiarrhythmic effect, influence on conductivity, contractility, excitability, automatism. Indications, contraindications and precautions, adverse reactions, pharmacokinetics;

b. Subclass IB (lidocaine group): antiarrhythmic effect, indications, contraindications and precautions, adverse reactions, pharmacokinetics;

c. Subclass IC (flecainide group): antiarrhythmic effect, indications, contraindications and precautions, side effects, pharmacokinetics.

5. Calcium channel blockers (class II): antiarrhythmic effect, indications, contraindications and precautions, adverse reactions.

6. Potassium channel blockers (drugs that mainly increase the effective refractory period - class III). Amiodarone: antiarrhythmic and antianginal effect, indications, contraindications, adverse reactions, pharmacokinetics. The particularities of sotalol and bretylium tosylate.

7. Drugs that reduce the tone of adrenergic innervation: classification.

8. Beta-blockers: antiarrhythmic effect, influence on the heart. The indications.

9. Antiarrhythmic drugs from various groups (analogues of nucleosides, cardiac glycosides, potassium drugs, magnesium drugs, etc.)

10. Antiarrhythmic drugs used in brady arrhythmias and atrioventricular block: classification, mechanism of action, effects, indications.

F. Individual works for the student's self-training (points 1, 2, 3 and 4 and are done in written form during the preparation process)

1) To prescribe the following drugs in all medicinal forms:

1. Quinidine. 2. Procainamide. 3. Lidocaine. 4. Mexiletine. 5. Flecainide. 6. Verapamil. 7. Amiodarone. 8. Sotalol. 9. Metoprolol. 10. Propranolol. 11. Potassium chloride.

Nr.	***Drug name***	***Dosage, medicinal forms***
1.	**Quinidine**	Tab. 0,1; 0,2
2.	**Procainamide**	Tab. 0,25 Sol. 10% - 5 ml in amp.
3.	**Lidocaine**	Sol. 2%; 10% - 5 ml in amp. (i/v)
4.	**Mexiletine**	Caps. 0,05; 0,2 Sol. 2,5% - 10 ml in amp.
5.	**Flecainide**	Tab. 0,05; 0,1
6.	**Verapamil**	Tab. / Caps. 0,04; 0,12; 0,24 Sol. 0,25% - 1 ml; 2 ml in amp.
7.	**Amiodarone**	Tab. 0,2 Sol. 5% - 3ml in amp.
8.	**Sotalol**	Tab. 0,08; 0,16 Sol. 1% - 4 ml in amp. Sol. 1,5% - 10 ml in vials
9.	**Metoprolol**	Tab. 0,025; 0,05; 0,1 Sol. 0,1% - 5 ml in amp.
10.	**Propranolol**	Tab. / Caps. 0,04; 0,08 Sol 0,1%- 1 ml in amp.
11.	**Potassium chloride**	Tab. 0,5; 0,1 Sol. 4% - 100 ml in vials Sol. 4% - 10 ml in amp.

2) List the groups and drugs used in (for): membrane stabilizers in supraventricular and ventricular arrhythmias; ventricular tachyarrhythmias of sympatho-adrenal (neurogenic) type; tachy systolic atrial flutter and fibrillation, ventricular arrhythmias; digital arrhythmias (cause by cardiac glycosides overdose); ventricular arrhythmias in myocardial infarction; rebellious supraventricular and ventricular arrhythmias to other antiarrhythmics; ventricular arrhythmias refractory to other antiarrhythmics; sinus bradycardia; atrio-ventricular block; cardiac arrest.

3) Tables (knowledge consolidation)

Table 1

Adverse reactions of antiarrhythmic drugs

Adverse reactions	IA	IB	IC	II (Ca^{2+}CB)	III (amio-darone)	β -AB
Reduction of myocardial contractility						
Bradicardia, AV block						
Arterial hypotension						
Headache						
Bronchospasm						
Haematotoxicity						
Hipo- / hyperthyroidism						
Deposition of microcrystals on the						

retina						
Alveolitis, pulmonary fibrosis						
Proarrhythmic effect						

Note: the presence of the effect is indicated by the "+" sign.

Table 2

The comparative characteristic of antiarrhythmic preparations

Parameters		Group of antiarrhythmic drugs					
		IA	IB	IC	II (Ca^{2+}CB)	III (amio-daronE)	β-AB
Blocking	Na channels						
	K channels						
	Ca channels						
Influence on the action potential of Purkinje fibers	phase 0						
	phase 1						
	phase 2						
	phase 3						
	phase 4						
	action potential duration						
Influence on heart parameters	automaticity						
	excitability						
	conductibility						
	contractility						
	duration of the effective refractory period						
Efficacy in arrhythmias	supraventricular						
	ventricular						

Note: to complete the table use the following signs:

"↑" - increase, "↓" - decrease, "-" - lack of effect, "+" - presence.

4) Problem of situation

In experimental conditions, a myocardial infarction was modeled with the development of ventricular fibrillation. The drug of choice was administered to suppress the ventricular fibrillation, which restored the normal rhythm.

What antiarrhythmic drug was indicated for this purpose?

What is the mechanism of action and effects on the heart?

What other groups and antiarrhythmic drugs can be used in ventricular arrhythmias?

5) Tests for self-training (Guide for laboratory work in pharmacology).

G. Interactive activity

1. Experimental and virtual didactic movie (conclusions).

2. Clinical cases (Guide for laboratory works in pharmacology).

3. Virtual situations (Guide for laboratory works in pharmacology).

ANTIANGINAL DRUGS

A. Actuality. Ischemic heart diseases (ischemic heart disease or coronary insufficiency) are the most frequent causes of disability and mortality of patients. For the treatment of these pathologies, are used drugs that improve the work of the heart and coronary circulation, blood coagulability and myocardial metabolism.

B. The purpose of the training is: familiarization of the student with the pharmacological properties of antianginal drugs, emergency medical care problems (treatment and prophylaxis of angina pectoris attacks, principles of drug treatment of acute myocardial infarction).

C. Learning objectives:

a) The student **must know:** the definition, classification, mechanism of action, effects, indications, contraindications and adverse reactions of antianginal drugs, the principles of treatment in acute myocardial infarction, the optimal routs of administration and the principles of dosing depending on the situation.

b) The student **must be able to:** prescribe in all forms of delivery the mandatory preparations from this group and list the groups and drugs in the respective diseases and pathological conditions.

D. Knowledge from previous and related disciplines necessary for interdisciplinary integration.

Human anatomy. Vascularization and innervation of the heart. Functional anatomy of the cardiovascular system.

Histology and embryology. Cardiovascular system. Blood vessels. The general principles of structure. Arteries. The vessels of the microcirculatory bed. The veins. Heart. Development, structure, histophysiology.

Physiology. Cardiac output, venous return and their regulation. Muscle blood flow and cardiac output in exercise, coronary circulation.

Pathophysiology. Etiology, pathogenesis, compensatory reactions and manifestations of cardiogenic-non-coronarogenic, coronarogenic, metabolic, hematogenous circulatory insufficiency.

Semiology - internal medicine. Notion about ischemic heart diseases. Risk factors of ischemic heart diseases. The main clinical forms of angina pectoris (stable, unstable, mixed, vasospastic angina (Prinzmetal). Acute myocardial infarction.

E. Self-training questions:

1. Definition and classification of antianginal drugs.
2. Drugs that decrease myocardial oxygen demand and increase oxygen supply: classification.
3. Organic nitrates. Molecular and systemic mechanism of action, pharmacological effects. Indications. Contraindications. Adverse reactions (early and late). Pharmacokinetics.
4. Sydnones (molsidomine group): molecular and systemic mechanism of action, pharmacodynamic advantages, indications, adverse reactions.
5. Calcium channel blockers: classification, molecular and systemic mechanism of action, pharmacological effects. Indications. Contraindications. Adverse reactions. Pharmacokinetics.
6. Second-line antianginal drugs: antianginal action and indications of ivabradine, ranolazine, nicorandil.
7. β-adrenergic blockers as antianginal drugs: classification, antianginal effect. Indications. Contraindications. Adverse reactions.
8. Drugs that increase oxygen supply (coronary vasodilators): mechanisms of action, effects, indications.
9. Cardioprotective drugs: mechanism of action, antianginal effect, indications.

10. Groups of drugs used for the treatment of acute myocardial infarction. Principles of action.

F. Individual works for the student's self-training (points 1, 2, 3 and 4 and are done in written form during the preparation process)

1) To prescribe the following drugs in all forms of delivery:

1. Nitroglycerin. 2. Isosorbide dinitrate. 3. Molsidomine. 4. Propranolol. 5. Nebivolol. 6. Nifedipine. 7. Verapamil. 8. Dipyridamole.

Nr.	***Drugs name***	***Dosage form, dose***
1.	**Nitroglycerine**	Tabl. 0,0005 (sublingual) Aerosol 1% - 10 ml (sublingual) Sol. 0,1% - 5 ml in amp. Sol. 0,1% - 50 ml in vials
2.	**Isosorbide dinitrate**	Tabl./ Caps. 0,02; 0,04 Sol. 0,1% - 10 ml in amp.
3.	**Molsidomine**	Tabl. 0,002; 0,004; 0,008
4.	**Nifedipine**	Tabl. 0,01; 0,02 Sol. 2% - 25 ml in vials (internal)
5.	**Verapamil**	Tabl. 0,04; 0,08; Caps. 0,12; 0,24 Sol. 0,25% - 2 ml in amp.
6.	**Nebivolol**	Tabl. 0,005
7.	**Propranolol**	Tabl./ Caps. 0,01; 0,04; 0,08 Sol. 0,1% - 1 ml in amp.
8.	**Dipiridamol**	Tabl/ Dragee 0,025; 0,075 Sol. 0,5% - 2 ml in amp.

2) List the groups and drugs used in (for): treatment of angina pectoris attacks; prophylaxis of angina pectoris attacks; 1st line medicines that are used in treatment of angina pectoris; 2nd line medicines that are used in treatment of angina pectoris; drugs to reduce the need for oxygen in angina pectoris; cardioprotective drugs in angina pectoris; pain relief in acute myocardial infarction; fear relief in acute myocardial infarction; thrombosis prophylaxis in acute myocardial infarction.

3) Tables (knowledge consolidation)

Table 1

Groups of drugs used in the treatment of acute myocardial infarction

Purpose of pharmacotherapy	Drugs group	Drugs
Reduce pain syndrome		
Removing arrhythmias		
Thrombosis prophylaxis and treatment		
Stimulation of myocardial contractile function		
Improved cardiac circulation		
Pulmonary edema therapy		

Table 2

Side effects of antianginal drugs

Adverse reactions	Nitrogly-cerine	Propranol ol	Nifedipine	Verapamil	Dipiridamol
Headache					
Vertigo					
Tachycardia					

Bradicardia					
Hypotension					
Bronhospasm					
Maleolar oedema					
Facial skin hyperemia					
The"stealing" phenomenon					
Withdrawal syndrome					

Note: the presence of the effect is indicated by a "+" sign.

Table 3

Tissue selectivity of calcium channel blockers

Chemical structure	Drugs	Predominant blockage of calcium channels:		
		Cardiomyocytes	Peripheral arterial vessels	Cerebral arterial vessels
Dihydropyridine derivatives				
Phenylalkylamine derivatives				
Benzothiazepine derivatives				
Diphenylpiperazine derivatives				

Note: use the following signs to complete the table:
"↑" - increase, "↓" - decrease, "-" - no effect.

Table 4

Mechanism of action of various groups of antianginal drugs

Principles of treatment of ischemic heart disease	Effects	Nitrates	β-AB	Ca^{2+}CB	Dipyridamole
Decreasing myocardial O2 demand by:	lowering of preload				
	lowering of afterload				
	lowering of HB				
Increased O2 supply to the myocardium by:	dilation of the coronary vessels of large caliber				
	dilation of the coronary vessels of small caliber				
	improvement of subendocardial circulation				
	blocking the central levels of coronaryoconstrictor reflexes				

Note: the presence of the effect is indicated by a "+" sign.

4) Problem of situation

Two patients with acute pain sensation in the region of the heart were hospitalized. Until the address, they had used sublingually on their own a drug which caused a non-essential pain relief and a cold sensation in the oral cavity. In admission department preparation A was administered sublingually to one patient in tablet form and to another in aerosol form. The pains subsided, but shortly afterwards palpitations, vertigo, facial hyperemia and headache occurred. Objective examination showed tachycardia (100 beats per minute) and a fall in BP to 100/60 mmHg.

What drug did the patients use for self-medication and the mechanism of action?
Which drug A was used in the hospital?
What is the cause of the adverse effects observed?
What other drugs could they use if they cannot tolerate preparation A?
5) Tests for self-training (Guide for laboratory work in pharmacology).

G. Interactive activity
1. Experimental and virtual didactic movie (conclusions).
2. Clinical cases (Guide for laboratory works in pharmacology).
3. Virtual situations (Guide for laboratory works in pharmacology).